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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MITOTIC KINESIN BINDING SITE

(57) Abstract: The present invention is directed to the identification, characterization and three-dimensional structure of a novel ligand binding site of KSP. Binding of ligands to the novel binding site result in a conformational change in the three-dimensional structure of the protein and a modulation of the activity of KSP. This conformational change in turn results in the formation of a novel binding pocket in the KSP protein, which comprises the novel binding site of the instant invention.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21145

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 9/00; C07K 17/00; C12Q 1/00, 1/34; G06F 19/00
US CL : 435/4, 18, 183; 530/350; 702/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/4, 18, 183; 530/350; 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	TURNER et al. Crystal structure of the mitotic spindle kinesin Eg5 reveals a novel conformation of the neck-linker. J. Biol. Chem. 06 July 2001, Vol. 276, No. 27, pages 25496-25502, see abstract.	56-58 ——— 1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.
Y	KULL et al. Crystal structure of the kniesin motor domain reveals a structural similarity to myosin. Nature. 11 April 1996, Vol. 380, pages 550-555, see abstract.	1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.
X — Y	BLANGY et al. Phosphorylation by p34cdc2 regulated spindle association of human Eg5, a kinesin-related motor essential for biopolar spindle formation in vivo. Cell. 29 December 1995, Vol. 83, pages 1159-1169, see abstract.	56-58 ——— 1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.
Y	US 5,221,410 A (KUSHNER et al.) 22 June 1993, see abstract.	1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.
Y	US 6,267,935 B1 (HOL et al.) 31 July 2001, see abstract.	1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.
Y	US 5,419,278 A (CARTER) 30 May 1995, see abstract.	1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A — Y	ROSSMANN et al. Application of crystallography to the design of antiviral agents. Infectious Agents and Disease. 1992, Vol. 1, pages 3-10, see abstract.	1-12 ——— 19-28, 30, 31, 34, 35, 40, 43-45.
A	WESS, T. J. Biochrystallography, structure determination, and beyond. Biotechnol. Appl. Biochem. 1997, Vol. 26, pages 127-142, see abstract.	1-12, 19-28, 30, 31, 34, 35, 40, and 43-45.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21145

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-12, 19-28, 30, 31, 34, 35, 40, and 56-58

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/21149

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, 19-28, 30, 31, 34, 35, 40, 43-45, and 56-58 drawn to a crystallized complex of human kinesin spindle protein (KSP), a method of identifying an agent that interact the ligand binding site of KSP, and the polypeptide of SEQ ID NO: 1.

Group II, claim(s) 13-15, drawn to a ligand binding site of KSP.

Group III, claim(s) 16-18, 29, 32, 33, 37, 38, 41, 42, 46, 47, 50-55, and 62-74, drawn to an agent that binds to the binding site of KSP.

Group IV, claim(s) 36, drawn to a method of identifying an anti-mitotic agent.

Group V, claim(s) 39, drawn to a method of determining the three dimensional structure of KSP complex.

Group VI, claim(s) 48-49, drawn to method of identifying inhibitor of KSP by utilizing the PSK tryptophan fluorescence.

Group VII, claim(s) 59-61, drawn to an active structure motif and a method of use.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature for the invention of Group I is the crystalline complex which is different from the ligand binding site of Group II, the chemical compounds of Group III, the atomic coordinates of Group V, the tryptophan fluorescence of KSP of Group VI, and the active site structure motif. While the special technical feature of the invention of Group IV is a crystalline KSP complex, the method of Group IV represents a second use for the KSP crystal complex. The special technical feature for the invention of Group III is the compound that binds to the binding site of the KSP, which are different from those of Groups IV-VII. The special technical features of the methods of Group IV-VI are the crystal complex of Group IV, the atomic coordinates of Group V, and the tryptophan fluorescence of KSP of Group VI, respectively, which differ from the active site structure motif of Group VII. Thus, the inventions of Groups I-VII lack unity of invention.

Continuation of B. FIELDS SEARCHED Item 3:

STN: Medline, Caplus, Scisearch, Lifesci, Biosis, Embase; WEST: PGPB, USPT, USOC, EPAB, JPAB, DWPI.
Sequence Search of SEQ ID NO: 1 in commercial data bases, issued US patent, and published US application.